REMARKS

Claims 1-11 and 14-16 are pending in this application. Claims 1-11 and 14-16 are canceled herein without prejudice. New Claims 17-29 are presented herein. Support for these new claims is found in the original claim language and throughout the specification, as set forth below. No new matter is added by the new claims and their entry is respectfully requested.

In light of these new claims and the following remarks, Applicants respectfully request reconsideration of this application and allowance of the pending claims to issue.

I. Claim 8

Claim 8, drawn to an invention nonelected with traverse, is contained in the application. Claim 8 has been canceled thereby addressing the Examiner's request.

II. Defective Declaration

The original declaration was objected to for failure to identify the city and either state or foreign residence of each inventor and for alterations that were not initialed or dated. *See* Final Office Action, page 2. Applicants have enclosed a new declaration with the present response, which corrects the inadvertent mistakes of the original declaration. Applicants respectfully request entry of this document.

III. Objection to the Abstract

The abstract was objected to as not being descriptive of the invention. *See* Final Office Action, page 2. The abstract has been amended by adding the sentence: "BiP levels can be increased above endogenous levels by over-expressing BiP or calreticulin." This amendment is believed to address the concerns of the Examiner, and Applicants respectfully request that the objection to the abstract be withdrawn.

IV. Rejection under 35 U.S.C. § 112, first paragraph

A. Enablement

Claims 1-7, 10-11 and 14-16 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate with the scope of the claims. *See* Final Office Action, page 3-4.

Claims 1-7, 10-11 and 14-16 are canceled herein without prejudice, thereby mooting this rejection, and Applicants respectfully request its withdrawal.

B. Written Description

Claims 1-7, 9-10 and 14-16 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Final Office Action states that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. *See* Final Office Action, page 5.

Claims 1-7, 9-10 and 14-16 are canceled herein without prejudice, thereby mooting this rejection, and Applicants respectfully request its withdrawal.

V. Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-7, 9-11 and 14-16 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly failing to point out and distinctly claim the subject matter of the invention. *See* Final Office Action, page 5-6.

Claims 1-7, 9-11 and 14-16 are canceled herein without prejudice, thereby mooting this rejection, and Applicants respectfully request its withdrawal.

VI. Rejection under 35 U.S.C. § 102

A. Claims 1-2 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Crofts et al. (*Plant Cell* 10:813-823, 1998). *See* Final Office Action, page 6-7.

Claims 1-2 are canceled herein without prejudice, thereby mooting this rejection, and Applicants respectfully request its withdrawal.

B. Claims 1-4, 10-11 and 14-15 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Arora et al. (*Physiol. Planta.* 103:24-34, 1998). *See* Final Office Action, page 8.

Claims 1-4, 10-11 and 14-15 are canceled herein without prejudice, thereby mooting this rejection, and Applicants respectfully request its withdrawal.

C. Claims 1-4, 10-11 and 14-15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Zhang et al. (*Protoplasma* 171:142-152, 1992). *See* Final Office Action, page 8.

Claims 1-4, 10-11 and 14-15 are canceled herein without prejudice, thereby mooting this rejection, and Applicants respectfully request its withdrawal.

VII. Rejection under 35 U.S.C. § 103(a)

A. Claims 1-7, 10-11 and 14-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Crofts et al. (*Plant Cell* 10:813-823, 1998). See Final Office Action, page 9.

Claims 1-7, 10-11 and 14-15 are canceled herein without prejudice, thereby mooting this rejection, and Applicants respectfully request its withdrawal.

B. Claims 9 and 16 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Crofts et al. (*Plant Cell* 10:813-823, 1998) and in further view of Denecke et al. (*Plant Cell* 7:391-406 (1995). *See* Final Office Action, page 9-10.

Claims 9 and 16 are canceled herein without prejudice, thereby mooting this rejection, and Applicants respectfully request its withdrawal.

C. Claims 1-4, 6, 10-11 and 14-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Coughlin et al. (U.S. Pat. No. 6,171,864). *See* Final Office Action, page10.

Claims 1-4, 6, 10-11 and 14-15 are canceled herein without prejudice, thereby mooting this rejection, and Applicants respectfully request its withdrawal.

VIII. Amendments to the Specification (Examples)

Amendments were made to several of the Examples to correct clerical errors and inadvertent mistakes made when the figures were referenced.

Example 6

Example 6, page 17, lines 37 through page 18, line 1, refers to Figure 7 and is now amended to refer to Figure 6. The discussion in Example 6 concerns treatment with tunicamycin. Figure 6 illustrates tunicamycin treatment and is the correct figure to be referenced here.

Example 11

Example 11, page 20, lines 31-32 refers to Figure 10 and is now amended to refer to Figure 11. Here, the Example 11 discussion concerns induction of BiP and PR1 expression following treatment of a *sail* mutant with salicylic acid. This is depicted in Figure 11, not in Figure 10.

Example 11, page 20 lines 34 through page 21, line 2, refers to Figure 10 and is amended to refer to Figure 7. Here, Example 11 compares BiP and PR1 expression in tobacco to that of the Arabidopsis *sail* mutant, following treatment with salicylic acid. Figure 7 illustrates expression profiles for BiP and PR1 in tobacco in response to salicylic acid treatment. Thus, Figure 7 is the figure that should be referred to in this instance.

Example 12

Example 12, page 21, lines 19-21, refers to Figure 11 and is amended to refer to Figure 12. Example 12 discusses BiP and PR1 expression in BiP-overproducing transgenic plants as compared to wild-type plants . This is illustrated in Figure 12 not Figure 11.

Example 12, page 21, lines 21-24, refers to Figure 11 and is amended to refer to Figure 12. Here, Example 12 also compares transgenic BiP overproducing tobacco plants with wild-type plants. This is illustrated in Figure 12, not Figure 11.

Example 13

Example 13, page 21, line 35 through page 22, line 1, refers to Figure 12A and is amended to refer to Figure 13A. The reference in Example 13 is to a plasmid construct. Figure 13A depicts the plasmid construct as discussed in Example 13.

Example 13, page 22, lines 4-7, refers to Figure 12B and is amended to refer to Figure 13B. Here, Example 13 discusses the effect of tunicamycin on α-amylase and GUS activity. This is illustrated in Figure 13B.

Example 14

Example 14, page 22, lines 33-34, refers to Figure 13A and is amended to refer to Figure 14A. Example 14 discusses correlations of α-amylase activity with GUS activity which is illustrated in Figure 14 A.

Example 14, page 22, lines 35-36, refers to Figure 12 and is amended to refer to Figure 14B. Example 14 discusses PAT coexpression. This is depicted in Figure 14B and not Figure 12.

Example 14, page 23, lines 2-5, refers to Figure 13B and is amended to refer to Figure 14B. Here, Example 14 discusses the effects of BiP overexpression and tunicamycin treatment on α-amylase activity. This is illustrated in Figure 14B and not Figure 13B.

Example 15

Example 15, page 23, lines 11-13, refers to Figure 14 and is amended to refer to Figure 15. Example 15 discusses transcripts levels. This is illustrated in Figure 15, not Figures 14A or 14B.

Example 15, page 23, lines 17-19, refers to Figure 12 and is amended to refer to Figure 15. Here, in Example 15 the discussion concerns the reduction in secretory protein synthesis. This is illustrated in Figure 15, not Figure 12A or 12B. Thus, the correct figure to be referenced in this instance is Figure 15.

Example 16

Example 16, page 23, line 25-27, refers to Figure 15A and is amended to refer to Figure16A. Example 16 discusses BiP overexpression in transgenic tobacco protoplasts and the effect of tunicamycin induced ER stress. This is illustrated in Figure 16A.

Example 16, page 23, lines 27-29, refers to Figure 15B and is amended to refer to Figure 16B. Here, Example 16 is discussing overexpression of a BiP derivative lacking an ER retention signal. Figure 16B illustrates the response of the BiP overexpressing derivative lacking an ER retention signal. Figure 15B does not exist.

IX. New Claims 17-29

New Claims 17-29 are presented herein for examination in this application and are directed toward a method of accelerating a plant's response to attack by a plant pathogen as recited therein. Support for these new claims is found throughout the specification, as noted above, and no new matter is added by these new claims.

Applicants believe that the new claims are free of the Examiner's prior rejections because these claims are directed to embodiments not deemed to be anticipated or rendered obvious by the references cited by the Examiner. Furthermore, Applicants believe that the subject matter of the new claims to be patentable in view of the declaration under 37 C.F.R. §1.132, provided by the inventor and submitted with this response.

Dr. Denecke states in his declaration that one skilled in the relevant art would recognize that multiple BiP's, both plant and non-plant, were known in the art at the time the present invention was filed. He also states that a high level of functional complementation was known to exist between the BiP from these various organisms. Thus, Applicants respectfully submit that the present invention would have been enabled for BiP's other than tobacco at the time of the filing. Additionally, it is noted that the specification of the present application, on page 14, line 1-4, discloses that BiP overproduction in potatoes causes resistance to soft rot.

Dr. Denecke further asserts that, rather than recognizing that increased BiP levels would lead to an accelerated response to pathogen attack, one of ordinary skill in that art would have concluded from the cited reference that increased BiP levels were instead the result of infection and increased production of defense-related proteins. Accordingly, Applicants respectfully submit that new Claims 17-29 are not anticipated or rendered obvious by the reference Crofts et al. (*Plant Cell* 10:813-823, 1998), and respectfully request that this rejection be withdrawn.

All of the issues raised in the Final Office Action are addressed herein. Thus, Applicants believe that the claims presented herein are free of the prior art and define patentable subject matter. The Examiner is invited and encouraged to contact the undersigned directly if such contact will expedite the prosecution of the pending claims to issue.

A check in the amount of $1320.00 ($980.00 as fee for a three month extension of time and $340.00 Notice of Appeal fee) is enclosed. This amount is believed to be correct; however the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account 50-0220.

Respectfully submitted,

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Susan E. Freedman

Susan E. Freedman
Date of Signature: November 8, 2004

Attorney Docket No. 9052-84 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Jurgen Denecke
Serial No.: 09/868,434 Group Art Unit: 1638
Filed: June 15, 2001 Examiner: A. Kubelik

For: *ENHANCING PLANT PATHOGEN RESISTANCE VIA INCREASING BIP LEVELS*

October 5, 2004

Commissioner for Patents
Post Office Box 1450
Alexandria, Virginia 22313-1450

DECLARATION UNDER 37 C.F.R § 1.132
OF JURGEN DENECKE, PhD.

Sir:

I, Jurgen Denecke PhD, do hereby declare and say as follows:

1. I received a Bachelor of Science degree (B.Sc) in Agricultural and Chemical Engineering from the University of Brussels, Belgium in 1986 and a Doctor of Philosophy degree (PhD.) from the University of Ghent in 1991. I am currently a Reader in the School of Biology at the University of Leeds, United Kingdom.

Additionally, I have delivered numerous lectures and authored and co-authored numerous articles and books in the areas of plant biotechnology, I am a named inventor for the present application and am knowledgeable of the contents of the above-identified patent application. I am also a co-author for the Crofts et al citation.

2. One of ordinary skill in the art of plant biochemistry would be apprised that at the time of filing the present application several non plant BiPs were in the public domain. For example BiPs had been identified in *Saccharomyces cerevisiae, Aspergillus*,

nematode worms, chicken, chinese hamsters and mice. BiPs were also known before December 1998 in *Arabidosis thaliana*, soybean, rice, maize, spinach and tobacco. (Please refer to Appendix I filed herewith for further details of BiPs in the public domain prior to December 1998). Therefore, the present application is adequately enabled for BiPs **other than** tobacco. Moreover, the high level of conservation was most rigorously demonstrated already in 1991 by my own experiments in which tobacco BiP was shown to functionally complement BiP in the yeast Saccharomyces cerevisiae. Tobacco BiP could fully replace the essential yeast BiP and sustain a viable strain (Denecke et al., 1991. The Plant Cell **3**, 1025-1035). One of ordinary skill in the art of plant biochemistry deduces from the high degree of conservation of BiP, even between kingdoms of organisms, that BiP from any eukaryotic cell, not just tobacco, would be sufficient to perform the invention. Indeed, even an artificially designed BiP which differs from any BiP in any given species would be appropriate so long as it possessed BiP **activity.**

I believe it would be possible for a competitor to develop plants and seeds from a plant over-expressing another BiP, for example a chicken BiP (see Appendix 1 example Stoeckle et al Mol. Cell. Biol. **8**, (7), 2675-2680, (1988)). This would bypass the present invention if it were limited to tobacco BiP. One of ordinary skill in the art of plant biochemistry would appreciate that a protein and its **activity** is what is crucial to the present invention **not** a nucleic acid sequence and a percentage of sequence identity.

Adequate definitions of "BiP Activity" are in the public domain and mainly illustrated in (Denecke et al., 1991. The Plant Cell **3**, 1025-1035) but also in (Leborgne-Castel et al., 1999. The Plant Cell **11**, 459-470). Indeed, the findings illustrated in Figure 12A on accelerated induction of PR1 (at 6 hours in BiP overproducers compared to 24 hours in wild type), or Figures 13 and 14 on the BiP-overexpression mediated resistance to the drug tunicamycin could also be used as routine methods of testing BiP **activity.**

Thus, in the present context, the specification supports the statement that the method of the present invention can be performed by over-expression of **any** BiP, not just plant BiPs and certainly not just BLP4.

3. I am a co-author of Crofts et al 1998, The Plant Cell, Vol 10, 813-823 May 1998. The disclosure in the paper does not recognise plants having increased levels of BiP or methods of increasing such protein levels would result in an accelerated response to pathogen attack or infection. Indeed, one of ordinary skill would have concluded that BiP induction may be a consequence of stress occurring from the increased production of defense related proteins. The opposite is shown to occur based on several key findings in the application as filed, including:

1) BiP gene induction occurs prior to the induction of defense-related proteins (Figure 1A) and is unrelated to the unfolded protein response (Figure 4). These findings were published and confirmed in Jelitto-Van Dooren et al., 1999. Plant Cell 11, 1935-1943, a date one year after the priority date of the present patent application and could not be deduced from the Crofts et al., 1998 disclosure.

2) An independent assay based on the plant signalling molecule salicylic acid showing that BiP synthesis occurs much earlier than PR1 synthesis and must therefore be due to a novel mechanism (Figure 7). This finding could not be deduced from Crofts et al., 1998 disclosure.

3) The finding that BiP over expression leads to accelerated induction of defence related proteins, illustrated by the complete induction of PR1 after merely 6 hours in BiP overproducing plants in contrast to 24 hours in wild type plants (Figure 12A), which led to the novel working model (Figure 17) which is the main foundation to the invention.

Such findings are not disclosed in Crofts et al 1998, The Plant Cell, Vol 10, 813-823 May 1998, moreover neither one of ordinary skill in the art of plant biochemistry or plant pathology, nor the authors of Crofts et al., 1998 themselves could have deduced or predicted such unexpected findings.

4. I believe that the present invention is not only fully supported for methods of overexpressing any BiP but that increased levels of BiP conferring a plant with an accelerated response time to pathogen attack is not disclosed in the prior art nor is the effect of BiP predictable.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Jürgen Denecke, PhD.

05/10/2004
Date

Appendix I Overview of BiP sequences in the public domain

AIa. Examples of non-plant BiPs published before filing in December 1998

Saccharomyces cerevisiae (brewers yeast)
Rose MD, Misra LM, Vogel JP.
KAR2, a karyogamy gene, is the yeast homolog of the mammalian BiP/GRP78 gene.
Cell. 1989 Jun 30;57(7):1211-21.

```
  1 mffnrlsagk llvplsvvly alfvvilplq nsfhssnvlv
 41 rgaddvenyg tvigidlgtt yscvavmkng kteilaneqg
 81 nritpsyvaf tdderligda aknqvaanpq ntifdikrli
121 glkyndrsvq kdikhlpfnv vnkdgkpave vsvkgekkvf
161 tpeeisgmil gkmkqiaedy lgtkvthavv tvpayfndaq
201 rqatkdagti aglnvlrivn eptaaaiayg ldksdkehqi
241 ivydlgggtf dvsllsieng vfevqatsgd thlggedfdy
281 kivrqlikaf kkkhgidvsd nnkalaklkr eaekakrals
321 sqmstrieid sfvdgidlse tltrakfeel nldlfkktlk
361 pvekvlqdsg lekkdvddiv lvggstripk vqqllesyfd
401 gkkaskginp deavaygaav qagvlsgeeg vedivlldvn
441 altlgiettg gvmtplikrn taiptkksqi fstavdnqpt
481 vmikvyeger amskdnnllg kfeltgippa prgvpqievt
521 faldangilk vsatdkgtgk sesititndk grltqeeidr
561 mveeaekfas edasikakve srnklenyah slknqvngdl
601 gekleeedke tlldaandvl ewlddnfeta iaedfdekfe
641 slskvaypit sklyggadgs gaadyddede dddgdyfehd
681 el
```

Aspergillus (filamentous mold)
Hijarrubia, M. J., Casqueiro, J., Gutierrez, S., Fernandez, F. J., and Martin, J. F.
Characterization of the bip gene of Aspergillus awamori encoding a protein with an HDEL retention signal homologous to the mammalian BiP
involved in polypeptide secretion.
Curr Genet 32, 139-46 (1997).

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  1 marishqgaa kpftawttif ylllvfiapl affgtahaqd
 41 etspqesygt vigidlgtty scvgvmqngk veilvndqgn
 81 ritpsyvaft deerlvgdaa knqyaanprr tifdikrlig
121 rkfddkdvqk dakhfpykvv nkdgkphvkv dvnqtpktlt
161 peevsamvlg kmkeiaegyl gkkvthavvt vpayfndaqr
201 qatkdagtia glnvlrvvne ptaaaiaygl dktgderqvi
241 vydlgggtfd vsllsidngv fevlatagdt hlggedfdqr
281 vmdhfvklyn kknnvdvtkd lkamgklkre vekakrtlss
321 qmstrieiea fhngedfset ltrakfeeln mdlfkktlkp
361 veqvlkdakv kksevddivl vggstripkv qalleeffgg
401 kkaskginpd eavafgaavq ggvlsgeegt gdvvlmdvnp
441 ltlgiettgg vmtkliprnt viptrksqif staadnqptv
481 liqvyegers ltkdnnllgk feltgippap rgvpqievsf
521 dldangilkv hasdkgtgka esititndkg rlsqeeidrm
561 vaeaeefaee dkaikakiea rntlenyafs lknqvndeng
```

601 lggqideddk qtildavkev tewlednaat attedfeeqk
641 eqlsnvaypi tsklygsapa deddepsghd el

Nematode worm
Wilson,R.
Genome sequence of the nematode C. elegans: a platform for investigating biology. The C. elegans Sequencing Consortium
JOURNAL Science 282 (5396), 2012-2018 (1998)

1 mktlfllgli alsavsvyce eeektekket kygtiigidl gttyscvgvy kngrveiian
61 dqgnritpsy vafsgdqgdr ligdaaknql tinpentifd akrligrdyn dktvqadikh
121 wpfkvidksn kpsvevkvgs dnkqftpeev samvlvkmke iaesylgkev knavvtvpay
181 fndaqrqatk dagtiaglnv vriineptaa aiaygldkkd gernilvfdl gggtfdvsml
241 tidngvfevl atngdthlgg edfdqrvmey fiklykkksg kdlrkdkrav qklrreveka
301 kralstqhqt kveieslfdg edfsetltra kfeelnmdlf ratlkpvqkv ledsdlkkdd
361 vheivlvggs tripkvqqli keffngkeps rginpdeava ygaavqggvi sgeedtgeiv
421 lldvnpltmg ietvggvmtk ligrntvipt kksqvfstaa dnqptvtiqv fegerpmtkd
481 nhqlgkfdlt glppaprgvp qievtfeidv ngilhvtaed kgtgnknkit itndqnrlsp
541 edierminda ekfaeddkkv kdkaearnel esyaynlknq iedkeklggk ldeddkktie
601 eaveeaiswl gsnaeasaee lkeqkkdles kvqpivskly kdagaggeea peegsddkde
661 l

Chicken
Stoeckle,M.Y., Sugano,S., Hampe,A., Vashistha,A., Pellman,D. and Hanafusa,H.
78-kilodalton glucose-regulated protein is induced in Rous sarcoma virus-transformed cells independently of glucose deprivation
Mol. Cell. Biol. 8 (7), 2675-2680 (1988)

1 mrhlllalll lggaraddee kkedvgtvvg idlgttyscv gvfkngrvei iandqgnrit
61 psyvaftpeg erligdaakn qltsnpentv fdakrligrt wndpsvqqdi kylpfkvvek
121 kakphiqvdv gggqtktfap eeisamvltk mketaeaylg kkvthavvtv payfndaqrq
181 atkdagtiag lnvmriinep taaaiaygld kregeknilv fdlgggtfdv slltidngvf
241 evvatngdth lggedfdqrv mehfiklykk ktgkdvrkdn ravqklrrev ekakralssq
301 hqarieiesf fegedfsetl trakfeelnm dlfrstmkpv qkvledsdlk ksdideivlv
361 ggstripkiq qlvkeffngk epsrginpde avaygaavqa gvlsgdqdtg dlvlldvcpl
421 tlgietvggv mtkliprntv vptkksqifs tasdnqptvt ikvyegerpl tkdnhllgtf
481 dltgippapr gvpqievtfe idvngilrvt aedkgtgnkn kititndqnr ltpeeiermv
541 ndaekfaeed kklkeridar nelesyaysl knqigdkekl ggklssedke tiekaveeki
601 ewleshqdad iedfkskkke leevvqpivs klygsagppp tgeeeaaekd el

Chinese Hamster
Ting,J., Wooden,S.K., Kriz,R., Kelleher,K., Kaufman,R.J. and Lee,A.S.
The nucleotide sequence encoding the hamster 78-kDa glucose-regulated protein (GRP78) and its conservation between hamster and rat
Gene 55 (1), 147-152 (1987)

1 mkfpmvaaal lllcavraee edkkedvgtv vgidlgttys cvgvfkngrv eiiandqgnr
61 itpsyvaftp egerligdaa knqltsnpen tvfdakrlig rtwndpsvqq dikflpfkvv
121 ekktkpyiqv digggqtktf apeeisamvl tkmketaeay lgkkvthavv tvpayfndaq
181 rqatkdagti aglnvmriin eptaaaiayg ldkregekni lvfdlgggtf dvslltidng
241 vfevvatngd thlggedfdq rvmehfikly kkktgkdvrk dnravqklrr evekakrals
301 sqhqarieie sffegedfse tltrakfeel nmdlfrstmk pvqkvledsd lkksdideiv
361 lvggstripk iqqlvkeffn gkepsrginp deavaygaav qagvlsgdqd tgdlvlldvc
421 pltlgietvg gvmtkliprn tvvptkksqi fstasdnqpt vtikvyeger pltkdnhllg
481 tfdltgippa prgvpqievt feidvngilr vtaedkgtgn knkititndq nrltpeeier
541 mvndaekfae edkklkerid trnelesyay slknqigdke klggklssed ketmekavee
601 kiewleshqd adiedfkakk keleeivqpi isklygsagp pptgeedtse kdel

Mouse

Kozutsumi,Y., Normington,K., Press,E., Slaughter,C., Sambrook,J. and Gething,M.J.
Identification of immunoglobulin heavy chain binding protein as glucose-regulated protein 78 on the basis of amino acid sequence, immunological cross-reactivity, and functional activity
J. Cell Sci. Suppl. 11, 115-137 (1989)

1 mmkftvvaaa llllgavrae eedkkedvgt vvgidlgtty scvgvfkngr veiiandqgn
61 ritpsyvaft pegerligda aknqltsnpe ntvfdakrli grtwndpsvq qdikflpfkv
121 vekktkpyiq vdigggqtkt fapeeisamv ltkmketaea ylgkkvthav vtvpayfnda
181 qrqatkdagt iaglnvmrii neptaaaiay gldkregekn ilvfdlgggt fdvslltidn
241 gvfevvatng dthlggedfd qrvmehfikl ykkktgkdvr kdnravqklr revekakral
301 ssqhqariei esffegedfs etltrakfee lnmdlfrstm kpvqkvleds dlkksdidei
361 vlvggstrip kiqqlvkeff ngkepsrgin pdeavaygaa vqagvlsgdq dtgdlvlldv
421 cpltlgietv ggvmtklipr ntvvptkksq ifstasdnqp tvtikvyege rpltkdnhll
481 gtfdltgipp aprgvpqiev tfeidvngil rvtaedkgtg nknkititnd qnrltpeeie
541 rmvndaekfa eedkklkeri dtrnelesya yslknqigdk eklggklsse dketmekave
601 ekiewleshq dadiedfkak kkeleeivqp iisklygsgg ppptgeedts ekdel

AIb. A selection of plant BiP sequences published before filing in December 1998

Cloning of tobacco BiP in 1991 was the first evidence for multigene families for this class of protein in plants, accompanied by functional complementation in the yeast Saccharomyces cerevisiae, which represents a cross-Kingdom complementation and demonstrates extreme functional conservation. Tobacco BiP contains 8 or more isoforms which are over 90% identical. The patent is based on experiments conducted on isoform 4 (BLP4), but the other isoforms are exchangeable. At the time of filing, it was clear to anybody in the field that functional complementation between a plant BiP and yeast BiP demonstrates functional conservation so that any BiP could be used.

Tobacco BiP isoform BLP4 (one of 8 cloned isoforms)
Denecke, J., Souza Goldman, M.H., Demolder, J., Seurinck, J. and Botterman, J. (1991). The tobacco lumenal binding protein is encoded by a multigene family. The Plant Cell **3**, 1025-1035.

```
   1 maggawnrrt slivfgivlf gclfafsiat eeatklgtvi gidlgttysc vgvyknghve
  61 iiandqgnri tpswvaftdg erligeaakn laavnpertv fdvkrligrk fddkevqrdm
 121 klvpykivnk dgkpyiqvki kdgetkifsp eeisamiltk mketaeaylg kkikdavvtv
 181 payfndaqrq atkdagviag lnvariinep taaaiaygld kkggeknilv fdlgggtfdv
 241 siltidngvf evlstngdth lggedfdqri meyfiklikk khgkdiskdn ralgklrrea
 301 erakralssq hqvrveiesl fdgvdfsepl trarfeelnn dlfrktmgpv kkamddagle
 361 ktqideivlv ggstripkvq qllkdyfdgk epnkgvnpde avaygaavqg gilsgeggde
 421 tkdillldva pltlgietvg gvmtkliprn tviptkksqv fttyqdqqtt vtiqvfeger
 481 sltkdcrllg kfdltgiapa prgtpqievt fevdangiln vkaedkasgk sekititndk
 541 grlsqeeier mvkeaeefae edkkvkerid arnsletyvy nmrnqindkd kladklesde
 601 kekietatke alewlddnqs aekedyeekl keveavcnpi itavyqksgg apggesgase
 661 dddhdel
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Arabidopsis thaliana (one of three isoforms in this species)
Koizumi, N.
Isolation and responses to stress of a gene that encodes a luminal binding protein in Arabidopsis thaliana
Plant Cell Physiol. 1996
Volume 37
862-865

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   1 marsfganst vvlaiiffgc lfafstakee atklgsvigi dlgttyscvg vyknghveii
  61 andqgnritp swvgftdser ligeaaknqa avnpertvfd vkrligrkfe dkevqkdrkl
 121 vpyqivnkdg kpyiqvkikd getkvfspee isamiltkmk etaeaylgkk ikdavvtvpa
 181 yfndaqrqat kdagviagln variinepta aaiaygldkk ggeknilvfd lgggtfdvsv
 241 ltidngvfev lstngdthlg gedfdhrime yfiklikkkh qkdiskdnka lgklrrecer
 301 akralssqhq vrveieslfd gvdlsepltr arfeelnndl frktmgpvkk amddaglqks
 361 qideivlvgg stripkvqql lkdffegkep nkgvnpdeav aygaavqggi lsgeggdetk
 421 dillldvapl tlgietvggv mtkliprntv iptkksqvft tyqdqqttvs iqvfegersl
 481 tkdcsllgkf dltgvppapr gtpqievtfe vdangilnvk aedkasgkse kititnekgr
 541 lsqeeidrmv keaeefaeed kkvkekidar naletyvynm knqvsdkdkl adklegdeke
 601 kieaatkeal ewldenqnse keeydeklke veavcnpiit avyqrsggap gaggesstee
 661 edeshdel
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Glycine max (Soybean)
Figueiredo,J.E.F., Cascardo,J.M., Carolino,S.M.B., Alvin,F. and Fontes,E.P.B.
Water-stress regulation and molecular analysis of the soybean BIP gene family
Braz. J. Plant Physiol. 9, 103-110 (1997)

1 magswarrsl ivlaiisfgc lfaisiakee atklgtvigi dlgttyscvg vyknghveii
61 annqgnritp swvaftdser ligeaaknla avnpertifd vkrligrkfe dkevqrdmkl
121 vpykivnkdg kpyiqvkikd getkvfspee isamiltkmk etaeaflgkk indavvtvpa
181 yfndaqrqat kdagviagln variinepta aaiaygldkk ggeknilvfd lgggtfdvsi
241 ltidngvfev latngdthlg gedfgqrime yfiklikkkh gkdiskdnra lgklrreaer
301 akralssqhq vrveieslfd gvdfsepltr arfeelnndl frktmgpvkk amedaglqks
361 qideivlvgg stripkvqql lkdyfdgkep nkgvnpdeav aygaavqegi lsgeggeetk
421 dillldvapl tlgietvggv mtkliprntv iptkksqvft tyqdqqttvs iqvfegersl
481 tkdcrllgkf dlsgippapr gtaqievtfe vdangilnvk aedkgtgkse kititnekgr
541 lsqeeiermv reekdfaeee kkvkeridar nsletyvynm knqvsdkdkl adklesdeke
601 kietavkeal ewlddnqsme kedyeeklke veavcnpiis avyqrsggap ggggasgeed
661 eddshdel

Rice
Muench,D.G., Wu,Y., Zhang,Y., Li,X., Boston,R.S. and Okita,T.W.
Molecular cloning, expression and subcellular localization of a BiP homolog from rice endosperm tissue
Plant Cell Physiol. 38 (4), 404-412 (1997)

1 mdrvrgsafl lgvllagslf afsvakeetk klgtvigidl gttyscvgvy knghveiian
61 dqgnritpsw vaftdserli geaaknqaav npertifdvk rdigrkfeek evqrdmklvp
121 ykivnkigkp yiqvkikdge nkvfspeevs amilgkmket aeaylgkkin davvtvpayf
181 ndaqrqatkd agviaglnva riineptaaa iaygldkkgg eknilvfdlg ggtfdvsilt
241 idngvfevla tngdthlgge dfdqrimeyf iklikkkysk diskdnralg klrreaerak
301 ralsnqhqvr veieslfdgt dfsepltrar feelnndlfr ktmgpvkkam ddagleksqi
361 heivlvggst ripkvqqllr dyfegkepnk gvnpdeavay gaavqgsils geggdetkdi
421 llldvapltl gietvggvmt kliprntvip tkksqvftty qdqqttvsiq vfegersmtk
481 dcrllgkfdl sgipaaprgt pqievtfevd angilnvkae dkgtgkseki titnekgrls
541 qeeidrmvre aeefaeedkk vkeridarnq letyvynmkn tvgdkdklad kleseekekv
601 eealkealew ldenqtaeke eyeeklkeve avcnpiisav yqrtggapgg rrrgrlddeh
661 del

Maize
Wrobel,R.L., OBrian,G.R. and Boston,R.S.
Comparative analysis of BiP gene expression in maize endosperm
Gene 204 (1-2), 105-113 (1997)

1 mdrvrgsafl lgvllagslf afsvakeetk klgtvigidl gttyscvgvy knghveiian
61 dqgnritpsw vaftdserli geaaknqaav npertifdvk rligrkfqdk evqrdmklvp
121 ykiinkdgkp yiqvkikdge nkvfspeeis amilgkmkdt aeaylgkkin davvtvpayf
181 ndaqrqatkd agviaglnva riineptaaa iaygldkkgg eknilvfdlg ggtfdvsilt
241 idngvfevla tngdthlgge dfdqrimeyf iklikkkysk diskdnralg klrreaerak
301 ralsnqhqvr veieslfdgt dfsepltrar feelnndlfr ktmgpvkkam edagleksqi
361 heivlvggst ripkvqqllk dyfngkepnk gvnpdeavaf gaavqgsils geggdetkdi
421 llldvapltl gietvggvmt kliprntvip tkksqvftty qdqqttvsiq vfegersmtk
481 dcrllgkfdl ngipsaprgt pqievtfevd angilnvkae dkgtgkseki titnekgrls
541 qeeidrmvre aeefaeedkk vkeridarnq letyvynmkn tvgdkdklad kleaeekekv
601 eealkealew lddnqsaeke dyeeklkeve avcnpivsav yqrsggapgg dadggvdddh

661 del

Spinach

Anderson,J.V., Neven,L.G., Li,Q.B., Haskell,D.W. and Guy,C.L.
A cDNA encoding the endoplasmic reticulum-luminal heat-shock protein from spinach (Spinacia oleracea L.)
Plant Physiol. 104 (1), 303-304 (1994)

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   1 mavawksras siafgivllg slfafvsakd eapklgtvig idlgttyscv gvykdgkvei
  61 iandqgnrit pswvaftnde rligeaaknq aaanpertif dvkrligrkf edkevqkdmk
 121 lvpykivnrd gkpyiqvkvq egetkvfspe eisamiltkm ketaetflgk kikdavvtvp
 181 ayfndaqrqa tkdagviagl nvariinept aaaiaygldk rggeknilvf dlgggtfdvs
 241 vltidngvfe vlatngdthl ggedfdqrlm eyfiklikkk htkdiskdnr algklrrece
 301 rakralssqh qvrveieslf dgvdfseplt rarfeelnnd lfrktmgpvk kamddaglek
 361 nqideivlvg gstripkvqq llkeffngke pskgvnpdea vafgaavqgs ilsgeggeet
 421 keillldvap ltlgietvgg vmtkliprnt viptkksqvf ttyqdqqttv tiqvfegers
 481 ltkdcrllgk fdltgiapap rgtpqievtf evdangilnv kaedkasgks ekititndkg
 541 rlsqeeierm vreaeefaee dkkvkekida rnsletyiyn mknqisdadk ladklesdek
 601 ekiegavkea lewlddnqsa ekedydeklk eveavcnpii tavyqrsggp sgesgadsed
 661 seeghdel
```